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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
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08/253,973 06/03/94 MCBRIDE

W 91875J

12M1/1113

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EXAMINER

HARTLEY, M

ART UNIT

PAPER NUMBER

1211

12

DATE MAILED:

11/13/96

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

- ☒ Responsive to communication(s) filed on 1-4-96 and 5-25-96
- ☐ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 1-36 is/are pending in the application.
- Of the above, claim(s) 11-25, 27, 30 and 32-36 is/are withdrawn from consideration.
- ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- ☒ Claim(s) 1-10, 26 and 31 is/are rejected.
- ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- ☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☐ Notice of Reference Cited, PTO-892
- ☒ Information Disclosure Statement(s), PTO-1449, Paper No. 6 (4 sheets)
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

- SEE OFFICE ACTION ON THE FOLLOWING PAGES -

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Applicant's election with traverse of Group I, claims 1-3, 5, 6, 26 and 31, wherein the elected species is identified as P829 and having the formula shown in table VI in the specification on page -48- in Paper No. 8 is acknowledged. The traversal is on the ground(s) that the groups are related as being drawn to reagents for preparing radiopharmaceuticals comprising specific radiometal binding moieties covalently linked to a targeting moiety, preferably a peptide; and that the rationale for defining the groups on the basis of their different Patent Office system of classification is unclear to Applicants. It is noted that the traversal was directed only to Groups I-IV. This is not found persuasive because the claims of group I are directed to a compound which is a monoamine, diamide, thiol-containing metal chelating group, or radiometal binding moiety, wherein the compound is defined as a heteroatom containing organic compound having the chemical structure as shown claim 2, as defined by the R groups. However, Groups III and IV are directed to compositions comprising specific amino acid peptide sequences with respect to the targeting moiety, wherein the radiometal binding moiety may be incorporated into a peptide having a sequence of specifically defined amino acids. Because these claims are actually drawn to the targeting moiety and not the radiometal binding moiety, as are Groups I and II, they are directed to different inventions. Also, the claims of Groups III and IV are directed to specific amino acid sequences, thus the claimed subject matter has acquired a separate status in the art as shown by their different classification. The classification of compositions comprising peptides defined by specific amino acid structure has acquired a separate status by the Patent Office classification system, classified in Class 530, subclass 300+. While subject matter comprising

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heteroatom containing organic compounds, such as metal chelators, has acquired a separate status in the art and is classified in Class 558, subclass 254. Because the subject matter has acquired a separate status in the art as shown by their different classification, it would constitute an undue burden on the examiner to search the subject matter of the previously designated groups.

The oversight on the part of the examiner of not grouping claim 4 has been acknowledged, thus claim 4 has been combined with the Applicant's elected group I and will be examined on its merits. Additionally, in reviewing the restriction requirement, the examiner has decided to collapse Groups I and II because the claims of both groups are directed to the metal chelator binding moiety. Thus, the elected Group I now contains group II, (i.e. claims 1-10, 26 and 31).

The requirement is still deemed proper and is therefore made FINAL.

It is suggested that in claim 1, the recitation of "that is" is changed to a more clear and concise terminology which is associated with defining the reagent, such as 'comprising' or 'consisting of', to help clarify what is actually claimed. Also, claim 2, which depends on claim 1, recites "A composition of claim 1", however, claim 1 is drawn to a reagent. It is suggested that the dependent claims are changed to directly read upon the subject matter to which the independent claims are directed.

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-10, 26 and 31 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fritzberg (USP 4,965,392, PTO-1449, dated 6-4-96) in combination with Rhodes (WO/12819, PTO-1449, dated 6-4-96).

The claims of the present invention appear to be directed to a monoamine, diamide, thiol-containing metal chelator covalently linked to a targeting moiety, having the formula as shown in claim 2.

Fritzberg discloses compositions used as reagents for preparing radiopharmaceutical agents comprising a chelating agent (radiometal binding moiety) such as a monoamine, diamide, thiol-containing chelator linked to a targeting moiety. Fritzberg discloses chelating agents having the structure in column 3 wherein X is, independently, H<sub>2</sub> or O. This formula may be substituted wherein two of the X substituents are O, and the remaining X is H<sub>2</sub>, thus the compound would be a monoamine, diamide, thiol-containing chelator similar to those of the instant claims, i.e. instant claim 2, formula (ii). Additionally, Fritzberg discloses that the chelating agent may be conjugated to polypeptides, antibodies, hormones, etc. as a specific binding moiety, see abstract and column 4.

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Rhodes discloses reagents for preparing radiopharmaceutical agents comprising medically useful metal ion-binding domains (radiometal binding moiety) linked to a peptide containing a biological-function domain (targeting moiety), see abstract. The medically useful metal-ion binding domain may include a monoamine, diamide, thiol-containing metal chelating structure which is derived from a variety of amino acids. The metal-ion binding domain is of the formula  $[Y_1-(R_1)-Y_1]$ , wherein  $Y_1$  may be amino acids including cysteine, arginine, penicillamine, etc, and  $(R_1)$  may be any amino acid sequence between 0-20 amino acids in length. Thus, the monoamine, diamide, thiol-containing metal-ion binding domain disclosed by Rhodes may comprise compositions having a structure corresponds to the amino acid sequence Lys-Cys-Arg which is similar to the structure of Applicants elected metal-binding moiety elected species and is encompassed by the formula of instant claim 2.

Although Fritzberg and Rhodes may not specifically disclose all of the exact monoamine, diamide, thiol-containing metal chelating agents which are linked to the same targeting moieties of the present claims, it would have been obvious to one of ordinary skill in the art to synthesize such monoamine, diamide, thiol-containing metal chelator covalently linked to a targeting moiety because Fritzberg and Rhodes disclose formulae which may be substituted to yield various monoamine, diamide, thiol-containing metal chelating agents, such as, various amino acid sequences which are modified to yield medically useful metal-ion binding domains which may be linked to various specific targeting moieties to gain the advantage providing various reagents

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which are useful for preparing a radiopharmaceutical agent, which may be specifically targeted to a desired site *in vivo* for treatment or diagnosis.

No claims are allowed at this time.


Note, the effective filing date for the claim subject matter was determined as the filing date of the instant application, 06-03-94, because support for the subject matter as drawn to the elected species was not found in the claimed priority document. Applicant is requested to state where specific support for the elected species can be found in the claimed priority document, in order for this date to be effective.

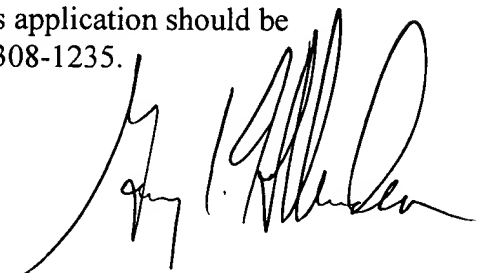
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Michael Hartley whose telephone number is (703) 308-4411. The examiner can usually be reached on Monday through Friday from 7:30 am to 4:00 pm in the eastern time zone. The facsimile numbers for group 1200 are (703) 308-4556 or (703) 305-3592.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Kight, III, SPE 1211 can be reached on (703) 308-0204.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Date: 11-7-96

Hartley/



GARY E. HOLLINDEN, PH.D.  
PRIMARY EXAMINER  
GROUP 1200